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EXAMINER	
HARRIS, ALANA M	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 05/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/934,025	BECKMANN ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-30 and 43-48* is/are pending in the application.

4a) Of the above claim(s) *18- 20 and 31-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *21-30 and 43-47* is/are rejected.

7)☒ Claim(s) *48* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

DETAILED ACTION

Response to Amendment and Arguments

1. Claims 18-40 and 43-48 are pending.

Claims 1-17, 41 and 42 have been cancelled.

Claim 22 has been amended.

Claims 47 and 48 have been added.

Claims 19, 20 and 31-40, drawn to non-elected inventions are withdrawn from examination.

Claims 21-30 and 43-48 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

3. The rejection of claims 22 and 27 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

New Objections

Specification

4. The disclosure is objected to because of the following informality: it contains several amino acid sequences not properly identified with a SEQ ID number, see page 4, lines 14 and 15; page 7, lines 10-12; page 12, lines 25 and 26. 37 CFR 1.82(d) requires the use of the assigned sequence identifier (SEQ ID NO) in all instances where the description of a patent application refers to a sequence and whenever a sequence or fragment thereof is claimed (see MPEP 2422.03). Correction is required.

Claim Objections

5. Claim 47 is objected to because of the following informality: the claim contains an amino acid sequence not properly identified with a SEQ ID number. Correction is required.

Maintained and New Grounds of Rejections

Claim Rejections - 35 USC § 112

6. Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.**

Applicants have amended claim 22 to include the recitation "A method of *modifying a dose of a B-tubulin modifying agent* that is administered to a patient,". The

italicized citation in particular is not supported by the specification. Applicants note in the Remarks submitted November 12, 2004 that support can be found in the original claim and at page 2, line 32 bridging to page 3, line 6, see page 7 of Remarks. This section of the disclosure has been reviewed and the concept of changing or modifying the dose of B-tubulin is neither of record nor the guidelines of how the dosage is altered. This section of the specification cites a method of monitoring the amount of B-tubulin isotype in a patient comprising the steps listed in claim 21. This designated section of the specification does not include the new method listed in the amended claim. Applicants should delete the new matter or properly identify where support can be found for this new method of modifying a dose of B-tubulin modifying agent.

7. The rejection of claim 27 under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials is maintained.

Applicants note they have amended the specification to provide the ATCC deposit information where available and "the claims will be amended to recite deposit information" upon identification of allowable claims, see Remarks, page 8, first sentence. These points of view have been considered, but found unpersuasive.

Applicants have added new claim 48 listing monoclonal antibody, 2C1H7 and its corresponding ATCC accession number. However, Applicants still need to file an

affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. The 2C1H7 antibody as well as the other antibodies listed in claim 27 do not have the requisite deposit information. Consequently, the rejection is maintained for the reasons of record, see first action on the merits (FAOM) mailed November 12, 2004, page 2, paragraph 4.

Claim Rejections - 35 USC § 103

8. The rejection of claims 21-30 and 43-47 under 35 U.S.C. 103(a) as being unpatentable over Shan et al. (Proc. Natl. Acad. Sci. USA 96: 5686-5691, May 1999/ IDS reference AE, submitted August 21, 2001), and further in view of WO 98/05315 (February 12, 1998/ IDS reference AC, submitted August 21, 2001), U.S. Patent number 4,517,288 (issued May 14, 1985) and Harlow and Lane (Antibodies, A Laboratory Manual, pages 319, 321-325 and 340-352, 1988) is maintained.

Applicants argue that passages cited by the Examiner do not provide proper support for the instant invention. Applicants submit "...the antibodies are able to detect

β-tubulin labeled with tritiated T138067", however they cite "there is no evidence that they specifically bind to modified β-tubulin, and not unmodified β-tubulin." , see Remarks, page 9. Applicants aver the Examiner's arguments provide no motivation and "assuming *arguendo* that one of skill had a motivation to try the antibodies of Shan et al...., the Examiner provides no convincing line of reasoning [the antibodies] would reasonably be expected to work in the manner set forth in the claims"., see page 10. These arguments and points of view have been carefully considered, but found unpersuasive.

It is clear from the teachings of Shan that T138067 modifies a subset of β-tubulin isotypes, see page 5688, column 2, "T138067 modifies..." section. Moreover, Shan clearly notes that "...various β-tubulin isotypes were detected with isotype-specific antibodies...", see page 5688, column 2, "T138067 modifies..." section. 3H-T138067 definitively modified Cys-239 of β_2 and β_4 tubulin isotypes and modified the β1 tubulin isotype at a reduced level, see page 5686, column 2, paragraph before the "Materials..." section. This subset of isotypes was detected with disclosed isotype-specific antibodies. These antibodies are reasonably concluded to be the same as Applicants, especially in light of the specification not listing deposit information for 1F6D8, 1B2C11, 3A1C11, 3F2A4, 5FC11, 6D4D11, 3D12D1, 4B6G6, 5F1D4, 6H8E3, 6H10C7, 3E10A3, 6A7F9 and 6E7G1.

It is clear to one of ordinary skill in the art that given the facts presented above and of record that the disclosed antibodies would be able to monitor the amount of modified β tubulin. Applicants have not provided evidence that would dissuade one of

ordinary skill in the art that the antibodies of Shan are not the same as Applicants. Absent evidence to the contrary the teachings of Shan (methodology and amino acid sequence) in combination with the secondary references read on Applicants' claimed methods, as well as the peptide presented in new claim 47. The Examiner has provided facts:

(a) T138067 modifies β_1, β_2 and β_4 tubulin isotypes at cysteine residue at position 239, see page 5686, column 2, last paragraph before "Materials..."section;

(b) isotype-specific antibodies bound T138067 modified β tubulin isotypes and "T138067 displays cytotoxic effects against MDR [mudltidrug-resistance] cells in culture and in mouse xenograft models", see page 5686, column 2, last paragraph before "Materials..." section.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention to establish a method of monitoring the amount of β–tubulin isotype in a patient treated with T1380670, as well as modifying the dose of T1380670 because pentafluorobenzensulfonamide compositions have demonstrated pharmacological activity in *in vitro* and *in vivo* assays with the adjustment of doses, see WO document, page 27, line 6-page 28, line 18 and it is clear that T1380670 had antitumor efficacy in mouse xerograph models, see page Shan, page 5691, "T138067 Is Efficacious...." section. One of ordinary skill in the art would have been motivated to combine all of the listed teachings in order to determine efficacy of specific doses of T138067 and thereby establish its clinical usefulness in the human treatment of MDR tumors, see abstract of Shan.

Furthermore the ability of T138067 to modify β-tubulin and evade cellular mechanisms of MDR provides the impetus to one of ordinary skill in the art to assay modified B-tubulin isotypes in a patient treated with an agent such as T138067 with specific antibodies in order to evaluate the therapeutic efficiency and toxicity of this potential anticancer agent for multi-drug resistant tumors.

Allowable Subject Matter

9. Claim 48 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The examiner works a flexible schedule, however she can normally be reached between the hours of 6:30 am to 5:30 pm with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
26 April 2006